Art Unit: ***

CLMPTO 7-10-03 LST

A derivative of an antibody, comprising a monoclonal antibody or the antibody fragment thereof which specifically reacts with ganglioside GD3 which is conjugated with a radioisotope, a protein or a low molecular weight agent.

- 2. The derivative of an antibody according to claim 1, wherein the monoclonal antibody which specifically reacts with ganglioside GD3 is an antibody selected from an antibody produced by a hybridoma, a humanized antibody and a human antibody.
- (Amended) The derivative of an antibody according to claim 1, wherein the
 monoclonal antibody comprises CDR1, CDR2 and CDR3 of H chain V region having the
 amino acid sequences represented by SEQ ID NOs:3, 4 and 5, respectively.
- 4. (Amended) The derivative of an antibody according to claim 1, wherein the monoclonal antibody comprises CDR1, CDR2 and CDR3 of L chain V region having the amino acid sequences represented by SEQ ID NOs:6, 7 and 8, respectively.
- 5. (Amended) The derivative of an antibody according to claim 1, wherein the monoclonal antibody comprises:

CDR1, CDR2 and CDR3 of a heavy chain (H chain) variable region (V region) having the amino acid sequences represented by SEQ ID NOs:3, 4 and 5, respectively; and

CDR1, CDR2 and CDR3 of a light chain (L chain) V region having the amino acid sequences represented by SEQ ID NOs:6, 7 and 8, respectively.

BEST AVAILABLE COPY

Application/Control Number: 10/089,500
Art Unit: ***

- 6. The derivative of an antibody according to claim 2, wherein the antibody produced by a hybridoma is RM641 (FERM BP-3116).
- 7. The derivative of an antibody according to claim 2, wherein the humanized antibody is a human chimeric antibody or a human CDR-grafted antibody.
- 8. The derivative of a human chimeric antibody according to claim 7, wherein the human chimeric antibody comprises an 8 chain V region and an L chain V region of a monoclonal antibody against ganglioside GD3 produced by a hybridoma.
- 9. The derivative of a human chimeric antibody according to claim 7, wherein the human chimeric antibody comprises:

an H chain V region and an L chain V region of a monoclonal antibody produced against ganglioside GD3 by a hybridoma; and

an E chain constant region (C region) and an L chain C region of a human antibody.

- (Amended) The derivative of a human chimeric antibody according to claim
 wherein the H chain V region comprises the amino acid sequence represented by
 SEQ ID NO:55.
- (Amended) The derivative of a human chimeric antibody according to claim
 wherein the L chain V region comprises the amino acid sequence represented by
 SEQ ID NO:56.

Art Unit: ***

12. (Amended) The derivative of a human chimeric antibody according to claim 8, wherein

the H chain V region comprises the amino acid sequence represented by SEQ ID NO:55; and

the L chain V region comprises the amino acid sequence represented by SEQ ID NO:56.

 (Amended) The derivative of a human chimeric antibody KM871 according to claim 8, wherein

the H chain V region comprises the amino acid sequence represented by SEQ ID NO:55; and

the L chain V region comprises the amino acid sequence represented by SEO ID NO:56.

- 14. The derivative of a human CDR-grafted antibody absording to claim 7, wherein the human CDR-grafted antibody comprises CDR of an H chain V region and an L chain V region of a monoclonal antibody against ganglioside GD3.
- 15. The derivative of a human CDR-grafted antibody according to claim 7, wherein the human CDR-grafted antibody comprises:

CDRs of an H chain V region and an L chain V region of a monoclonal antibody against ganglioside GD3; and

framework regions (FRs) of an H chain V region and an L chain V region of a human antibody.

16. The derivative of an antibody according to claim 7, whorein the human CDR-grafted antibody comprises:

CDRs of an H chain V region and an L chain V region of a monoclonal antibody against ganglioside GD3;

FRs of an H chain V region and an L chain V region of a human antibody; and

an Π chain C region and an L chain C region of a human antibody.

Art Unit: ***

- 17. (Amended) The derivative of a human CDR-grafted antibody according to claim 14, wherein the antibody comprises CDR1, CDR2 and CDR3 of the H chain V region having the amino acid sequences represented by SEQ ID NOs:3, 4 and 5, respectively.
- 18. (Amended) The derivative of a human CDR-grafted antibody according to claim 14, wherein the antibody comprises CDR1, CDR2 and CDR3 of the L chain V region having the amino acid sequences represented by SEQ ID NOs:6, 7 and 8, respectively.
- 19. (Amended) The derivative of a human CDR-grafted antibody according to claim 14, wherein the antibody comprises:
- CDR1, CDR2 and CDR3 of the H chain V region having the amino acid sequences represented by SEQ ID NOs:3, 4 and 5, respectively; and
- CDR1, CDR2 and CDR3 of the L chain V region having the amino acid sequences represented by SEQ ID NOs:6, 7 and 8, respectively.
- 20. (Amended) The derivative of a human CDR-grafted antibody according to claim 14, wherein the H chain V region of the antibody comprises the amino acid sequence represented by SEQ ID NO:9.
- 21. (Amended) The derivative of a human CDR-grafted antibody according to claim 14, wherein the L chain V region of the antibody comprises the amino acid sequence represented by SEQ ID NO:54.
- 22. (Amended) The derivative of a human CDR-grafted antibody according to claim 14, wherein the H chain V region and the L chain V region of the antibody comprises the amino acid sequences represented by SEQ ID NO:9 and SEQ ID NO:54, respectively.

Art Unit: ***

23. (Amended) The derivative of a human CDR-grafted antibody KM8871 according to claim 14, wherein

the H chain V region of the antibody comprises the amino acid sequence represented by SEQ ID NO:9; and

the L chain V region of the antibody comprises the amino acid sequence represented by SEQ ID NO:54.

- 24. The derivative of the antibody fragment according to claim 1, wherein the antibody fragment is an antibody fragment selected from Fab, Fab', F(ab'), a single chain antibody (scFv), a disulfide stabilized V region fragment (dsFv) and a peptide comprising CDR.
- 25. (Amended) The derivative of the antibody fragment according to claim 1, wherein the antibody fragment comprises amino acid sequences of an H chain V region and an L chain V region of a monoclonal antibody against ganglioside GD3 produced by a hybridoma.
- 26. (Amended) The derivative of the antibody fragment according to claim 1, wherein the antibody fragment comprises an H chain V region of the antibody having the amino acid sequence represented by SEQ ID NO:55.
- 27. (Amended) The derivative of the antibody fragment according to claim 1, wherein the antibody fragment comprises an L chain V region of the antibody having the amino acid sequence represented by SEQ ID NO:56.
- 28. (Amended) The derivative of the antibody fragment according to claim 1, wherein the antibody fragment comprises:

Application/Control Number: 10/089,500 Art Unit: ***

an Hichain V region of the antibody having the amino acid sequence represented by SEO ID NO:55; and

an L chain V region of the antibody having the amino acid sequence represented by SEO ID NO:66.

29. (Amended) The derivative of the antibody fragment according to claim 1, wherein the antibody fragment comprises amino acid sequences of an H chain V region and an L chain V region of a human CDR-grafted antibody against ganglioside GD3.

30. (Amended) The derivative of the antibody fragment according to claim 1, wherein the antibody fragment comprises an H chain V region of the antibody having the amino acid sequence represented by SEQ ID NO:9.

- 31. (Amended) The derivative of the antibody fragment according to claim 1, wherein the antibody fragment comprises an L chain V region of the antibody having the amino acid sequence represented by SEQ ID NO:54.
- 32. (Amended) The derivative of the antibody fragment according to claim 1, wherein the antibody fragment comprises:

an H chain V region of the antibody having the amino acid sequence represented by SEQ (D NO:9) and

an L chain V region of the antibody having the amino acid sequence represented by SEQ ID NO:54.

አ

Art Unit: ***

- 33. (Amended) The derivative of an antibody fragment according to claim 1, wherein the antibody fragment comprises CDR1, CDR2 and CDR3 of an H chain V region of the antibody having the amino acid sequences represented by SEQ ID NOs:3, 4 and 5, respectively.
- 34. (Amended) The derivative of the antibody fragment according to claim 1, wherein the antibody fragment comprises CDR1, CDR2 and CDR3 of an L chain V region of the antibody having the amino acid sequences represented by SEQ ID NOs:6, 7 and 8, respectively.
- 35. (Amended) The derivative of the antibody fragment according to claim 1, wherein the antibody fragment comprises:
- CDR1, CDR2 and CDR3 of an H chain V region of the antibody having the amino acid sequences represented by SEQ ID NOs:3, 4 and 5; and
- CDR1, CDR2 and CDR3 of an L chain V region of the antibody having the amino acid sequences represented by SEQ ID NOs:6, 7 and 8.
- 36. (Amended) The derivative of a monoclonal antibody or the antibody fragment thereof according to claim 1, wherein the protein is a cytokine.
- 37. The derivative of a monoclonal antibody or the antibody fragment thereof according to claim 36, wherein the cytokine is human interleukin-2 (hIL-2).
- 38. The derivative of an antibody according to claim 37, wherein the derivative of an antibody comprises a human chimeric antibody KM871 and hIL-2.
- 39. The derivative of an antibody according to claim 38, wherein the antibody conjugated with hIL-2 comprises:
- an H Chain V region having the amino acid sequence represented by SEQ ID NO:57; and
- an L chain V region having the amino acid sequence represented by SEQ ID NO:56.

Art Unit: ***

- 40. The derivative of an antibody according to claim 37, wherein the derivative of an antibody comprises a human CDR-grafted antibody KM8871 and hIL-2.
- 41. The derivative of an antibody according to claim 1, wherein the antibody conjugated with hIL-2 comprises:
- an B chain V region having the amino acid sequence represented by SEQ ID NO:53; and
- an L chain V region having the amino acid sequence represented by SEQ ID NO:54.
- 42. (Amended) A DNA which encodes the derivative of a monoclonal antibody or the derivative of the antibody fragment thereof which specifically reacts with ganglioside GD3 according to claim 1.
- 43. A recombinant vector comprising the DNA according to claim 42.
- 44. A transformant which is obtained by introducing the recombinant vector according to claim 43 into a host cell.
- 45. A transformant KM871hIL2 (FERM BP-6918) which produces the antibody according to claim 38.
- 46. A transformant RM8871hIL2 (FERM BP-6791) which produces the antibody according to claim 40.
 - 47. (Amended) A process for producing an antibody, which comprises:

culturing the transformant according to claim 44 in a culture medium to produce and accumulate the derivative of a monoclonal antibody or the derivative of the antibody fragment thereof in the culture; and

recovering the derivative of the antibody or the derivative of the antibody fragment thereof from the culture.

Application/Control Number: 10/089,500
Art Unit: ***

- 48. A human CDR-grafted antibody or the antibody fragment thereof which specifically reacts with ganglioside GD3.
- 49. The human CDR-grafted antibody or the antibody fragment thereof according to claim 48, wherein the human CDR-grafted antibody comprises CDRs of an B chain V region and an L chain V region of a monoclonal antibody against ganglioside GD3.
- 50. The human CDR-grafted antibody or the antibody fragment thereof according to claim 48, wherein the human CDR-grafted antibody comprises:

CDRs of an H chain V region and an L chain V region of a monoclonal antibody against ganglioside GD3; and

FRs of an H chain V region and an L chain V region of a human antibody.

51. The human CDR-grafted antibody or the antibody fragment thereof according to claim 48, wherein the human CDR-grafted antibody comprises:

CDRs of an H chain V region and an L chain V region of a monoclonal antibody against ganglioside CD3;

PRs of an E chain V region and an E chain V region of a human antibody; and

an H chain C region and an L chain C region of a human antibody.

- 52. (Amended) The human CDR-grafted antibody or the antibody fragment thereof according to claim 49, wherein the antibody comprises CDR1, CDR2 and CDR3 of the H chain V region having the amino acid sequences represented by SEQ ID NOs:3, 4 and 5, respectively.
- 53. (Amended) The human CDR-grafted antibody or the antibody fragment thereof according to claim 49, wherein the antibody comprises CDR1, CDR2 and CDR3 of the L chain V region having the amino acid sequences represented by SEQ ID NOs:6, 7 and 8, respectively.
- 54. (Amended) The human CDR-grafted antibody or the antibody fragment thereof according to claim 49, wherein the antibody comprises:

Art Unit: ***

CDR1, CDR2 and CDR3 of the H chain V region having the amino acid sequences represented by SEO ID NOs:3, 4 and 5, respectively; and

CDR1, CDR2 and CDR3 of the L chain V region having the amino acid sequences represented by SEQ ID NOs:6, 7 and 8.

- 55. (Amended) The human CDR-grafted antibody or the antibody fragment thereof according to claim 49, wherein the H chain V region of the antibody comprises the amino acid sequence represented by SEQ ID NO:9.
- 56. (Amended) The human CDR-grafted antibody or the antibody fragment thereof according to claim 49, wherein the L chain V region of the antibody comprises the amino acid sequence represented by SEQ ID NO:54.
- 57. (Amended) The human CDR-grafted antibody or the antibody fragment thereof according to claim 49, wherein

the H chain V region of the antibody comprises the amino acid sequence represented by SEQ ID NO:9; and

the L chain V region of the antibody comprises the amino acid sequence represented by SEQ ID NO:54.

58. (Amended) The human CDR-grafted antibody KM8871 or the antibody fragment thereof according to claim 49, wherein

Art Unit: ***

the H chain V region of the antibody comprises the amino acid sequence represented by SEQ ID NO:9; and

the L chain V region of the antibody comprises the amino acid sequence represented by SEQ ID NO:54.

- 59. (Amended) A DNA which encodes the human CDR-grafted antibody or the antibody fragment thereof which specifically reacts with ganglioside GD3 according to claim 48.
- 60. A recombinant vector comprising the DNA according to claim 59.
- 61. A transformant which is obtained by introducing the recombinant vector according to claim 60 into a host cell.
- 62. A transformant KM9871 (FERM BP-6790) which produces the human CDR-grafted antibody according to claim 58.
 - 63. (Amended) A process for producing an antibody, which comprises:

culturing the transformant according to claim 61 in a culture medium to produce and accumulate the human CDR-grafted antibody or the antibody fragment thereof in the culture; and

recovering the antibody or the antibody fragment thereof from the culture.

- 64. (Amended) A medicament comprising at least one selected from the derivative of a monoclonal antibody and the derivative of the antibody fragment thereof according to claim 1 and the human CDR-grafted antibody and the antibody fragment thereof which specifically reacts with ganglioside GD3.
- 65. (Amended) A therapeutic agent for cancers, comprising, as an active ingredient, at least one selected from the derivative of a monoclonal antibody and the derivative of the antibody fragment thereof according to claim 1 and the human CDR-

Art Unit: ***

grafted antibody and the antibody fragment thereof which specifically reacts with ganglioside GD3.

66. (Amended) A diagnostic agent for cancers, comprising, as an active ingredient, at least one selected from the derivative of a monoclonal antibody and the derivative of the antibody fragment thereof according to claim 1 and the human CDR-grafted antibody and the antibody fragment thereof which specifically reacts with ganglioside GD3.

This Page is Inserted by IFW Indexing and Scanning Operations and is not part of the Official Record

BEST AVAILABLE IMAGES

Defective images within this document are accurate representations of the original documents submitted by the applicant.

Defects in the images include but are not limited to the items checked:
☐ BLACK BORDERS
☐ IMAGE CUT OFF AT TOP, BOTTOM OR SIDES
☐ FADED TEXT OR DRAWING
☐ BLURRED OR ILLEGIBLE TEXT OR DRAWING
☐ SKEWED/SLANTED IMAGES
☐ COLOR OR BLACK AND WHITE PHOTOGRAPHS
☐ GRAY SCALE DOCUMENTS
☐ LINES OR MARKS ON ORIGINAL DOCUMENT
☐ REFERENCE(S) OR EXHIBIT(S) SUBMITTED ARE POOR QUALITY
□ OTHER:

IMAGES ARE BEST AVAILABLE COPY.

As rescanning these documents will not correct the image problems checked, please do not report these problems to the IFW Image Problem Mailbox.